Journal of Surgical Oncology 61:63–65 (1996)

Syndrome of Inappropriate Antidiuretic Hormone Secretion in Papillary Serous Surface Carcinoma of the Peritoneum

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A case of syndrome of inappropriate antidiuretic hormone secretion (SIADH) in a patient with suboptimally cytoreduced stage III papillary serous surface carcinoma of the peritoneum is described. After the primary surgery, the patient refused further therapy. Within a month bilateral pleural effusions and abdominal ascites compelled the patient to accept treatment with carboplatin and cyclophosphamide. Ten days following the chemotherapy, she was admitted in a disoriented state with serum sodium of 117-mEq/L. During the evaluation, treatment, and subsequent follow-up, the diagnosis of SIADH was confirmed. Numerous disease processes have been associated with the development of SIADH; however, there have been few reports in gynecologic malignancies. Possible etiology and clinical management of this patient are briefly discussed.

KEY WORDS: SIADH, adenocarcinoma, gynecologic cancer

INTRODUCTION

SIADH has been well described as a paraneoplastic phenomenon and as a side effect of a variety of cytotoxic agents [1]. Although other tumor sites have been amply documented, there is a paucity of reports in gynecologic malignancies [2–4]. We relate the manifestation of SIADH in a patient with recurrent bilateral pleural effusions and ascites due to papillary serous surface carcinoma of the peritoneum.

CASE REPORT

A 71-year-old gravida 4, para 4, with a previously unremarkable medical history, was transferred to the gynecologic oncology service of our medical center. She presented to the outlying facility with acute shortness of breath and a computerized tomogram revealing left pleural effusion, ascites, omental tumor "caking," and soft tissue densities within the intraperitoneal fat. The patient underwent thoracentesis, total abdominal hysterectomy, bilateral salpingo-oophorectomy, and a cytoreductive effort. The size of the residual disease was > 2 cm. Final surgical-pathological diagnosis was Stage III, grade 3 papillary serous surface carcinoma of the peritoneum. The left pleural fluid, uterus, fallopian tubes, and ovaries were free of cancer.

Postoperative recovery was uneventful with complete resolution of her symptoms. The patient refused all further therapy and left for a vacation. Within 2 weeks, while out of state, she required emergent bilateral thoracentesis for symptomatic relief. The pleural fluid this time was found to contain papillary serous carcinoma compatible with the peritoneal primary. She returned home and received the first cycle of carboplatin and cyclophosphamide. Palliative thoracentesis had to be performed again.

Ten days following administration of chemotherapy, the patient was brought to the emergency department in an agitated and disoriented state. The abnormal laboratory data included serum sodium 117 mEq/L, serum osmolality 247 mOsm/kg, urine osmolality 256 mOsm/kg, and urine sodium 20 mEq/L. The diagnosis of SIADH was made; the patient was placed on free-water restric-

Accepted for publication August 8, 1995.
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tion. The patient's mental status improved; however, electrolyte abnormalities continued to worsen. Urine osmolality reached 544 mOsm/L, serum sodium decreased to 113 mEq/kg, and serum osmolality decreased to 240 mOsm/L. Replacement with 3% saline was instituted, as well as intravenous boluses of furosemide. Demeclocycline was added several days later because of slow recovery of serum sodium. In the meantime, the recurrent symptomatic left hydrothorax required a chest tube placement with subsequent pleurodesis.

Complete normalization of all electrolyte levels was achieved by the 20th day of hospitalization. The patient was treated with carboplatin and paclitaxel. She later received four more cycles of this combination without experiencing SIADH, or requiring free-water restriction and demeclocycline. She is alive with disease undergoing second-line chemotherapy treatment at 12 months of follow-up.

DISCUSSION

SIADH is a disorder in which excessive circulating levels of antidiuretic hormone (ADH) result in persistent hyponatremia and inappropriately concentrated urine. Since its first description in 1957 [5], an extensive list of disease processes associated with SIADH has been accumulated.

Cranial trauma and central nervous system (CNS) infections commonly produce SIADH. Pulmonary function disturbance caused by such inflammatory processes as pneumonia, cavitary tuberculosis, asthma, and mechanical ventilation may also result in increased pituitary secretion [1]. Some known sources of ectopic production of ADH are lung tumors, especially oat cell carcinoma. Other malignancies also appear to stimulate the neurohypophysis abnormally [6]. A variety of tumor sites have been reported, e.g., head and neck [7], pancreas [8], colon [9], bladder [10], prostate [11]. Gynecologic malignancies, however, appear to be underaccounted. We were able to find only three references [2–4] siting cervix, endometrium, and ovary.

Numerous chemotherapeutic agents have been implicated in the initiation of SIADH. Of particular significance in gynecologic malignancies is the finding that cisplatin [12], cyclophosphamide [13], ifosfamide [14], vincristine [15], vinblastine [16], and melphalan [17] are associated with the syndrome.

For most cases of acute SIADH, several days of free-water restriction will correct the metabolic abnormalities. Sodium chloride replacement is not required unless the patient exhibits CNS disturbances. Chronic SIADH is usually seen as a paraneoplastic phenomenon. For these patients, demeclocycline will inhibit ADH at the renal cell level, correcting hyponatremia on a long-term basis.

Although in this patient there was not enough evidence to establish categorically that the papillary serous surface carcinoma of the peritoneum was producing ADH ectopically, several other etiologies could be discussed. Drug-related cause of her SIADH was unlikely because of time of onset, slow resolution, and nonrecurrence with subsequent cycles. She had recurrent symptomatic pleural effusions requiring frequent drainage, so it is possible to suggest that an inflammatory lung process initiated increased pituitary secretion. Another feasible explanation is that due to frequent thoracentesis there was a state of ADH hypersecretion in response to decreased effective blood volume.

This case report confirms that in SIADH it is frequently difficult to establish the main contributing factor. Physicians treating patients with papillary serous surface carcinoma of the peritoneum should be aware of the possible association with SIADH in order not to delay the early diagnosis and treatment.

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